DETAILED ACTION

The Office action mailed 12-22-08 is HEREBY VACATED and a new Office action is set forth below.

This Office action is in response to the communications filed 11-6-08.

Claims 89-107 are pending in the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11-6-08 has been entered.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 101 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is being drawn to a composition comprising a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT, nucleotides 9-16 of SEQ ID NO. 9, and further comprising a polymer.

The specification, claims and the art do not adequately describe the distinguishing features or attributes concisely shared by the members of the genus comprising *polymers*.

The specification teaches various cell delivery compositions, including colloidal dispersions and encapsulating agents. The examples provided at the time of filing, therefore, are not representative or correlative of the genus comprising *polymers*. Concise structural features that could distinguish structures within this genus (e.g., Which members of the genus, *polymer*, are useful for cell or tissue delivery?) from others are missing from the disclosure. (*e.g.*, What is encompassed by the term polymer that provides utility for the instant claims?). No common structural attributes identify the members of the claimed genus, and distinguish members within the genus from those outside of the claimed genus. One of skill in the art would reasonably

conclude that the disclosure fails to provide a representative number of species to describe the genus claimed. Thus, Applicant was not in possession of the genus.

Claims 93, 104-107 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for tumor treatment following direct administration of a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT, nucleotides 9-16 of SEQ ID NO. 9, does not reasonably provide enablement for the treatment of any cancer comprising any route of administration of a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT, nucleotides 9-16 of SEQ ID NO. 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to methods of treating any cancer comprising any route of administration of a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT, nucleotides 9-16 of SEQ ID NO. 9.

The state of the prior art and the predictability or unpredictability of the art. Branch and Crooke teach that the in vivo (whole organism) application of molecules is a highly unpredictable endeavor due to target accessibility and delivery issues. Crooke also points out that cell culture examples are generally not predictive of *in vivo* inhibition of target molecules. (See entire text of A. Branch, Trends in Biochem. Sci., 23, 45-50,

1998; and S. Crooke, Ann. Rev. Med., Vol. 55, pages 61-95, 2004, esp. pages 71-72, 74, 81, 84-85).

Peracchi cites stability and delivery obstacles that need to be overcome in achieving desired in vivo efficacy: "A crucial limit of ribozymes in particular, and of oligonucleotide-based drugs in general, lies in their intrinsically low ability to cross biological membranes, and therefore to enter the cells where they are supposed to operate…cellular uptake following systemic administration appears to require more sophisticated formulations… the establishment of delivery systems that mediate efficient cellular uptake and sustained release… remains one of the major hurdles in the field." (See Peracchi et al, Rev. Med. Virol., 14, pages 47-64, 2004, abstract on page 47 and text on page 51).

Cellular uptake by appropriate target cells is a rate limiting step that has yet to be overcome in achieving predictable clinical efficacy. Both Chirila et al and Agrawal et al point to the current limitations which exist in our understanding of the cellular uptake of small molecules in vitro and in vivo (see Agrawal et al, Molecular Med. Today, Vol. 6, pages 72-81, 2000, especially at pages 79-80; see Chirila et al, Biomaterials, Vol. 23, pages 321-342, 2002, especially pages 326-327 for a general review of the important and inordinately difficult challenges of the delivery of therapeutic molecules to target cells).

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. The specification teaches the treatment of tumors in a subject comprising the direct intra-tumoral administration of SEQ ID No.

9. The specification fails to teach tumor reduction comprising the systemic administration of SEQ ID NO. 9. One skilled in the art would not accept on its face the examples given in the specification of direct administration and subsequent treatment effects on that tumor as being correlative or representative of the ability to provide for the treatment of all cancers in a subject comprising the systemic administration of SEQ ID NO. 9, or of any a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT. There is a lack of guidance in the specification and an unpredictability associated with the successful targeting and delivery of therapeutic oligonucleotides to appropriate target cells in an organism to provide the treatment effects broadly claimed.

The breadth of the claims and the quantity of experimentation required. The claims are drawn to methods of treating any cancer comprising any route of administration of a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT, nucleotides 9-16 of SEQ ID NO. 9, including the treatment of glioblastoma, medulloblastoma, neuroblastoma, melanoma or carcinoma. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of treatment effects for these cancers, including those requiring delivery of the therapeutic oligonucleotide through the blood brain barrier, or comprising administration other than direct intra-tumoral administration. Since the specification fails to provide sufficient guidance for the full scope claimed, and since determination of these factors is highly unpredictable, it would require undue experimentation to practice the invention over the full scope claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 89-107 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 6-9 of U.S. Patent No. 7,108,844 for the reasons of record set forth in the Office action mailed 10-5-07.

Applicant's arguments filed 3-5-08 have been fully considered but they are not persuasive. Applicant argues that the difference in scope between the instant claims and claims 1-9 of U.S. Patent No. 7,108,844 render them patentably distinct and therefore the instant rejection is improper.

The instant claims and claims 1-9 of U.S. Patent No. 7,108,844 are both drawn to methods of utilizing compositions for treating cancers in a subject comprising the administration of compositions comprising an immunomodulatory oligonucleotide

between 20-100 nucleobases in length and comprising SEQ ID No. 51, which encompasses the sequence AACGTTAT of the instant application, and includes SEQ ID Nos. 9, 10, 16, 21, 31, 33-35 of the instant application.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
12-29-08

/Jane Zara/

Primary Examiner, Art Unit 1635